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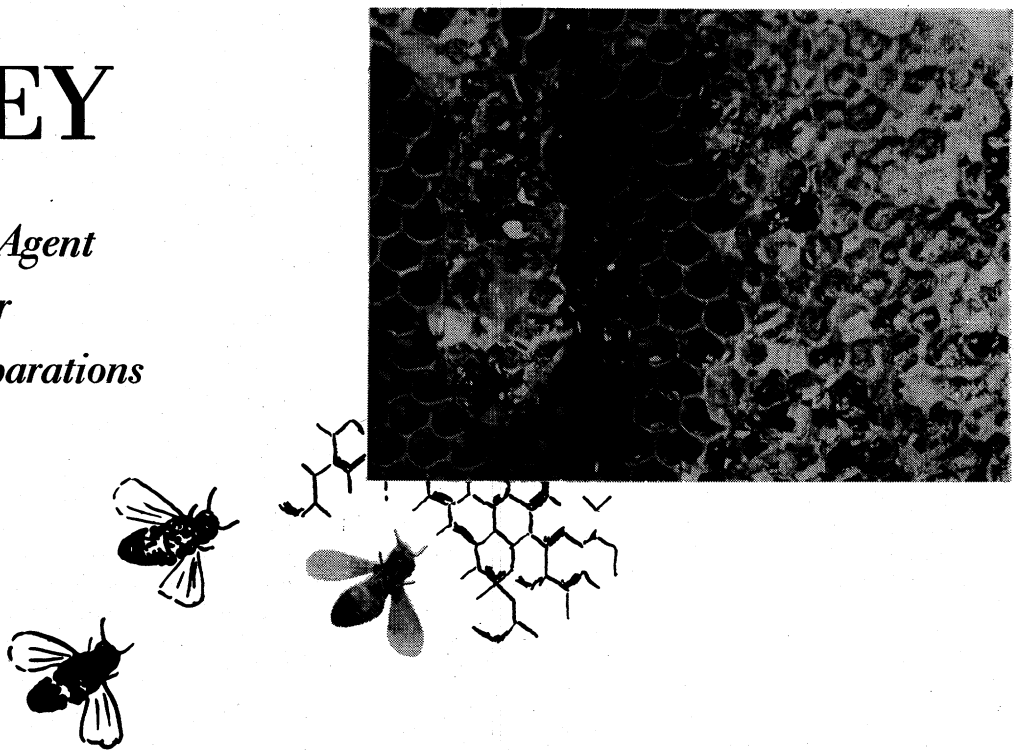
HONEY

... a flavoring Agent and Vehicle for Medicinal Preparations



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HONEY HAS LONG BEEN USED in the formulation of medicinal preparations, but little information regarding its suitability as a vehicle is available. The acquisition of such data was the object of a recently completed, two-year research program at the Philadelphia College of Pharmacy and Science, under a contract with the United States Department of Agriculture, supervised by the Eastern Utilization Research and Development Division of the Agricultural Research Service, and authorized by the Research and Marketing Act of 1946.

Twenty-one different types of medicinal preparations were investigated to determine if honey may replace all or part of the sugar syrup and/or glycerin normally used as vehicles. The problems of stability of the active constituent(s) in preparations containing honey, along with possible improvement of palatability by the pleasant natural flavor of honey, were of prime consideration. In some instances honey imparted both exceptional taste and high stability; in others it was of little or no utility as a vehicle. A summary of the principal findings follows.**

Stability of Honey Formulations

Honey is naturally acid in reaction, having a pH of about 3.7. Raising the pH tends to change both the color and aroma, the honey becoming darker and acquiring an unpleasant aroma, which is especially pronounced above pH 7. It is not desirable, therefore, to incorporate honey in any preparation which is alkaline.

The effect of temperature was also investigated, sample preparations being stored at room temperature, at 37° C. (98.6° F.), and at 50° C. (122° F.). At 50° C. honey containing 10% added water (the usual concentration used in this study) became very dark, at times developing a black precipitate. The unfavorable effect of elevated temperature is therefore quite apparent.

Since good pharmaceutical practice requires solutions to have a high degree of clarity, it is advantageous to use the commercial variety of honey designated as "heat-processed and filtered." The desirability of employing honey which does not require filtration to achieve clarity is readily apparent when this cumbersome operation on such a viscous fluid does have to be performed. It should be noted that even the clearest honeys show the turbidity characteristic of colloidal solutions. In preparing formulations with clear honey the general procedure usually involves only mixing a filtered aqueous solution of the water-soluble medicinal agents with the honey. For insoluble materials a suspending technique is utilized (see the Sulfonamide Suspension formulation).

Ferrous Sulfate Formulation

Honey proved to be an excellent vehicle for ferrous sulfate. A formulation prepared as specified for U.S.P. Ferrous Sulfate Syrup, usually made in sugar syrup

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**(A complete report of the findings of this investigation, including quality specifications, may be found in the *American Journal of Pharmacy*, Volume 131, July, 1959).

flavored with peppermint, is given below.

Ferrous Sulfate (hydrous)	40	Gm.
Citric Acid (hydrous)	2.1	Gm.
Water	210	Gm.
Honey*	1150	Gm.

This solution was extremely palatable, with practically no evidence of the astringency characteristic of many preparations containing iron.

Sulfonamide Suspension

For preparing suspensions, of the type of U.S.P. Oral Trisulfapyrimidine Suspension, honey is an ideal vehicle component. Not only may chemically stable suspensions be prepared, but they also show the desirable characteristics of slow settling, ease of uniform redispersion, and palatability. The following formulation ranked first in a taste preference "panel" of 25 students.

Sulfadiazine (Calcomites®)	42	Gm.
Sulfamerizine (Calcomites®)	42	Gm.
Sulfamethazine (Calcomites®)	42	Gm.
Sodium Citrate	6.7	Gm.
Acacia	6.7	Gm.
Methylparaben	0.5	Gm.
Propylparaben	0.11	Gm.
Alcohol	17	Gm.
Glycerin	170	Gm.
Honey	950	Gm.
Water, sufficient to make a total of	1350	Gm.

*(In order to know the exact compostion, most of our preparations were formulated by weight; this formula yields about one liter of solution).

This formula yields about one liter of suspension, and was prepared as follows: (1) The acacia was wetted with some water, the remainder of which was used to dissolve the sodium citrate; (2) the prabens were dissolved in alcohol; (3) the sulfonamides were mixed with the glycerin and honey; (4) to the sulfonamide suspension was added the parabens solutions; (5) to the mixture obtained in (4) the acacia and sodium citrate solutions were added, alternately; (6) the product was passed through a colloid mill. In place of the parabens 0.5% (w/v) of sorbic acid or its equivalent of potassium sorbate may be used as a preservative.

Cough Preparations

Honey has long been used in Europe as an ingredient for treatment of cough. Its viscosity makes it well suited for this purpose. Clinical use of a product of the following formulation indicated good antitussive action; the taste is excellent.

Dihydrocodeinone Bitartrate	0.32	Gm.
Pyrilamine Maleate	2.4	Gm.
Potassium Guaiacolsulfonate	32	Gm.
Sodium Citrate	16	Gm.
Citric Acid	16	Gm.
Sorbic Acid	0.5	Gm.
Water	160	Gm.
Honey	1150	Gm.

The solid ingredients were dissolved in about 140 Gm. of water with warming, the solution filtered and mixed with the honey. This formation yields about one liter of solution. Occasionally filtration, under pressure and using a filter aid, is necessary.

Terpin Hydrate Formulations

The following variant of the N.F. Terpin Hydrate Elixir, prepared in the same manner as the official product, was found to be of good flavor.

Terpin Hydrate	16.9	Gm.
Sweet Orange Peel Tincture	20	ml.
Alcohol	425	ml.
Glycerin	200	ml.
Honey	400	ml.
Water, sufficient to make	1000	ml.

At times a fine precipitate formed after standing for several weeks, which was easily removed by filtration by virtue of the viscosity of this preparation being considerably less than that of the honey formations previously described.

Aspirin Preparation

Suspensions of aspirin were very palatable, but not very stable. In two days 5% hydrolysis occurred, and in five days this had increased to 12%. Nevertheless, honey dispersions of aspirin may be well suited for administration to children if they are used within a day or two of compounding.

Other Preparations

Honey solutions of the more common water soluble vitamins were also studied. Riboflavin (Vitamin B_2), used in the form of sodium riboflavin-5'-phosphate, proved to be the most stable of the vitamins, provided the solution is stored in amber glass bottles. Thiamine (Vitamin B_1) is not as stable in honey as it is in some other vehicles, though in combination with riboflavin its stability is considerably improved. Ascorbic acid (Vitamin C) is less stable in honey than in simple syrup. Cyanocobalamin (Vitamin B_{12}) deteriorates very rapidly in consequence of the high carbohydrate content of honey.

Preservation Against Microorganisms

Honey diluted with water is subject to deterioration by microbiological growth. Part of this investigation had to do with the study of various preservatives which would inhibit such deterioration. This study indicated sorbic acid in 0.05% (w/v) concentration (or the equivalent concentration of the more soluble potassium sorbate) to be the most effective preservative, and it appears advisable to incorporate it in any preparation containing honey and water.

Quality Specifications

While standards for honey are provided in the monograph of the *National Formulary*, these standards will not insure constancy of different lots of honey. Uniformity is essential for different batches of product in which honey is an ingredient. Quality specifications must be quite restrictive for honey intended for use in medicinals. Briefly, honey for medicinal formulations should be of "U. S. Choice" or "U. S. Fancy" grade, contain not more than 18.6% moisture by weight, contain no artificial honey, and not be darker than light amber when graded by U.S.D.A. color standards.

Many floral types of honey are commercially available, the choice at the discretion of the manufacturer of the product containing the honey. (Clover honey was used in most of the formulations recorded in this paper). Regardless of floral type, the honey should meet all of the proposed requirements.

Acknowledgment

The authors are appreciative of the helpful suggestions and other aid of Dr. Jonathan W. White, Jr., of the Eastern Utilization Research and Development Division of the Agricultural Research Service.